

**Advisory Action
Before the Filing of an Appeal Brief**

Application No.

10/798,896

Applicant(s)

RABINOVSKY ET AL.

Examiner

Thaia N. Ton

Art Unit

1632

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 February 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: 17, 21-24, 26, 28, 29, 31, 33, 38 and 41-44.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Thaia N. Ton/
Primary Examiner, Art Unit 1632

Continuation of 11, does NOT place the application in condition for allowance because:

Claims 17, 21, 31, 33, 38 and 42 stand rejected under 35 U.S.C. 102(b) as being anticipated by Alila et al. (cited previously).

Applicants argue that the Alila reference fails to disclose a method to stimulate angiogenesis because they fail to disclose a subject with a muscle injury and fails to suggest stimulating angiogenesis, or growth of new blood vessels. In particular, Applicants argue that even if they describe a "muscle injury", a method to stimulate angiogenesis in such a subject by administration of a nucleic acid construct encoding IGF-I is not necessarily present in Alila, because they disclose effects of IGF-I on neurons when expressed in muscle tissue, and they teach the induction of GAP-43, a nerve-specific growth associated protein that is an indicator of motor neuron sprouting, not angiogenesis. Applicants argue that Alila does not teach or suggest that the genetic material encoding IGF-I when administered to a subject necessarily leads to stimulating angiogenesis because they only suggest this in treating affect muscles. See page 7 of the Response.

These arguments have been considered but are not found to be persuasive. In particular, Alila states that IGF-I plays an important role in the maintenance and regeneration of peripheral nerves and skeletal muscle and offers the potential to treat neuromuscular disease in humans (abstract). In particular, Alila teaches that muscle is an attractive site for the delivery and expression of exogenous genes to treat neuromuscular diseases (see p. 1785, col. 2, 1st paragraph). Alila additionally discuss using their method to treat local myoneuropathies. The Examiner provides the definitions of "myopathy" and "neuromuscular disease" (accessed online www.en.wikipedia.com, on March 10, 2009). In particular, a "myopathy" is a muscular disease in which the muscle fibers do not function for any one of many reasons, resulting in muscular weakness, and that a muscular disease can be classified as neuromuscular or musculoskeletal in nature (see first paragraph). In fact, some conditions, such as myositis can be considered both neuromuscular and musculoskeletal. See second paragraph. The term "neuromuscular disease" is a broad term that encompasses many different diseases and ailments that either directly or via nerve pathology, impair the functioning of the muscles. See first paragraph. For example, the article discusses that muscular dystrophy is a large group of diseases wherein muscle integrity is disrupted (see last paragraph, 1st page). Thus, given these definitions of "myopathy" and "neuromuscular disease", one of skill in the art would reasonably understand that Alila intends for their methods to be used in a variety of disease, including those diseases wherein muscle integrity is disrupted, for example, injured or malfunctioning. Thus, the Examiner maintains that Alila anticipates this aspect of the claimed invention. Finally, although Alila look at the effects of IGF-I on neurons, given that they teach injection into muscles, the property of stimulating angiogenesis is inherent to IGF-I. Given that Alila teach the same plasmid that is required by the instant claims, and that they teach injection into muscles, the property stimulating angiogenesis is inherent. Accordingly, Alila et al. teach the claimed invention, because they teach intramuscular injection of a construct with a myogenic promoter (chicken skeletal alpha-actin), which is operably linked to a nucleic acid sequence encoding IGF-I, operably linked to a 3'UTR region, and they teach the expression of this plasmid construct localized to muscle tissue. They anticipate claim 42 because Alila teach the human growth hormone 3'UTR.

Alila et al. further anticipate specific embodiments of the claims in that they teach delivery via a single administration (claim 31); delivery into muscle which are diploid cells (claim 33); and that the subject is an animal (rat) (claim 38).

In the instant case, Alila et al. teach the steps of injection of a specific nucleic acid expression construct which fulfills the limitations of the claims; thus, the property of the nucleic acid, when expressed, is that that it stimulates angiogenesis. Applicants have argued that "stimulation of angiogenesis" is not a "property" of the claimed nucleic acid sequence encoding IGF-I, but is a downstream physiological response to the expressed IGF-I in muscle. The Examiner responds that the Alila reference provides sufficient guidance to show that their construct expresses IGF-I in muscle tissue, therefore, it is reasonable to conclude that the property of the nucleic acid, when expressed, is that it would stimulate angiogenesis.

Accordingly, Alila et al. anticipate the claims..

Claims 22-23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Alila et al. further in view of van Deutekom et al. (Mol. Med. Today, 214-220, May 1998).

Applicants argue that the combination of Alila in view of van Deutekom cannot render the claimed invention obvious and present the same arguments, with respect to Alila, which have been addressed above. These arguments have been addressed above.

Claims 17, 24, 28, 29, 41, 43 and 44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Alila et al. (cited above) in view of Draghia-Akli (cited previously), Fewell et al (cited previously) and Isner (cited previously).

Applicants argue that the combination of Alila, Draghia-Akli and Fewell do not render the claimed invention obvious and argue the same arguments regarding the Alila reference, which have been addressed above.